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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/404,010	09/23/1999	YING LUO	A-68294/DJB/	7948

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
XIE, XIAOZHEN	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 07/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/404,010	LUO ET AL.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/25/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25 and 27-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25 and 27-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 25 April 2005 has been entered. Claims 25 and 27-33 are pending and under examination in this office action.

Response to Amendment

Applicant's arguments filed 25 April 2005 have been considered but they are not persuasive for new and remaining issues.

New and remaining issues are set forth below.

Claim Rejections - 35 USC § § 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 27-33 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for reasons of record set forth in the previous Office Actions (18 October 2004, 24 March 2004 and 22 September 2003).

The claims are drawn to a nucleic acid encoding a Mkinase protein. Applicant argues that Mkinase can be used for, e.g., TRAF4 detection or purification because Mkinase can bind to TRAF4 protein. Applicant argues that TRAF4 is a member of the tumor necrosis factor receptor factor family and TRAF proteins are known to regulate CD40 signaling through TRAF binding sites. The Sax and El-Deiry reference (J. Biol. Chem., 2003, Vol. 278, No. 38, pp. 36435-36444) teaches that TRAF family of adaptor proteins mediate cellular signaling by binding to various members of the tumor necrosis family receptor superfamily and interleukin-1/Toll-like receptor superfamily; however, in contrast to its other family members, TRAF4 has not been shown to bind to a member of the tumor necrosis family receptor superfamily *in vivo*, nor has it been shown to regulate signaling pathways common to its other family members (pp. 36435, abstract). Further, The Sax and El-Deiry reference teaches that TRAF4 knock out mice exhibit a phenotype distinct from other TRAF family member-deficient mice (pp. 36435, third paragraph). Therefore, the role of TRAF4 in a signaling pathway had not been established, and little is known about the biological function or regulation of TRAF4 as late as 2003, and required further study at that time, while the instant application has a filing date of September 23, 1999. Since there is no specific and substantial utility

associated with TRAF4, there is no "real world" use associated with "detection and purification" of a protein whose significance itself is unknown.

Applicant argues that Mkinase proteins and nucleic acids have asserted utility on their own because of the association of the chromosomal Mkinase gene with certain cancers. Applicant's argument have been fully considered but have not been found to be persuasive for reasons set forth in the previous Office Actions (18 October 2004, 24 March 2004 and 22 September 2003).

Applicant provides post-filing date evidence in the form of a report by Kato et al. that Mkinase protein gene maps to a region of chromosome 11 known to contain a breakpoint associated with germ cell tumors and renal carcinoma. There is no teaching in the specification that an artisan would identify a particular chromosome localization or any consequences of such localization. There is no guidance to indicate how the gene is associated with cancers, whether the gene is mutated or differencially expressed in any condition, including cancer. One skilled in the art would not be able, based on applicant's specification, to diagnose any cancer or obtain any prognostic information. What is provided is merely an idea for an invention and clearly, further research was necessary in order to identify how it would actually be used.

The instant application has provided a description of a protein, which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as diagnostic agents to detect cancer, the instant invention is incomplete. In the absence of knowledge of the biological significance of this protein, and the consequences of TRAF4

binding and chromosomal localization, there is no immediately obvious patentable use for it. Since the instant specification does not disclose a "real world" use for diagnostic agents to detect cancer, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

Claims 25, 27-33 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition, claims 30-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell in culture comprising a polynucleotide with the sequence as set forth in SEQ ID NO:1, does not reasonably provide enablement for *in vivo* transfection.

The specification on page 17 discloses that the nucleic acids of the current invention can be expressed in a wide variety of host cell types, including cells within a host animal. However, there are no actual or prophetic examples that disclose how to make or use host cells that comprise a DNA sequence as set forth in SEQ ID NO:1 in an animal. The Examiner cites Eck & Wilson (page 81, column 2, second paragraph to page 82, column 1, second paragraph) who report that numerous factors complicate *in vivo* gene expression which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume distribution,

rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. Since the instant disclosure does not address any of the methods necessary to make a host cell in an animal which comprises the polynucleotide of interest, the claims as written are not enabled. This rejection could be overcome by addition of the limitation wherein the host cells are isolated.

Conclusion

NO CLAIM IS ALLOWED.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D. whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
July 7, 2005

ROBERT S. LANDSMAN, PH.D.
PRIMARY EXAMINER